REMARKS

Justification for the amendments is as follows. Claims 1-3, 9-11, 16, 19, 21, 22 and 28 are amended to recite that the agent is a HIF prolyl hydroxylase inhibitor, support for which can be found throughout the specification, e.g., at paragraphs [0036] and [0037]. Support for newly added claims 48 and 49 can be found throughout the specification, e.g., at paragraphs [0037] and [0038].

Claims 6-8 and 39-45 are canceled herein without prejudice to their renewal. Applicants specifically reserve the right to prosecute the subject matter of the canceled claims in continuing or divisional applications.

No new matter is introduced by any of these amendments, and entry of the amendments is respectfully requested.

RESPONSE TO OFFICE ACTION

I. Claim Status

Claims 1-47 were originally filed and were subject to restriction. Applicants affirm below the election, with traverse, of Group 1, claims 1-36 and 39-45, for prosecution, of which claims 17, 18, 34 and 35 have been withdrawn from consideration by the Examiner based on election of species for examination. Applicants above amend claims 1-3, 9-11, 16, 19, 21, 22 and 28, add new claims 48 and 49, and cancel claims 6-8 and 39-45 without prejudice to their renewal. Thus, claims 1-5, 9-16, 19-33, 36-38, and 46-49 are currently pending.

II. Election/Restriction

The Examiner restricted the claims in the above-referenced application as follows:

Group I: Claims 1-36 and 39-45, drawn to a method for increasing endogenous gamma globin in a subject, the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin and drawn to a method for treating or pretreating a subject infected with or at risk for being infected with a species of Plasmodium, the method comprising increasing fetal hemoglobin level in the subject; and

Group II: Claims 37, 38, 46, and 47, drawn to a medicament comprising an agent which increases expression of the gene encoding gamma globin for use in increasing fetal hemoglobin level in a subject.

The Examiner also stated that the claims of Group I are directed to the following species:

1. Type of cell:
   - (a) Hematopoietic stem cells
   - (b) Blast-forming unit erythroid (BFU-E)
2. Second therapeutic agent
   - (a) hydroxyurea
   - (b) butyrate analogs
   - (c) 5-azacytidine
3. HIF hydroxylase enzyme selected from:
   - (a) EGLN
   - (b) FIH1

(c) PHD4

4. Species of disorder or condition:

(a) beta-thalassemia and sickle cell syndrome

(b) infection with Plasmodium

The Examiner required, if Applicants elect the claims of Group I for examination, further election of a single species from each category 1 to 4 above to which the claims shall be restricted if no generic claim is finally held to be allowable. The Examiner identified the following claims as generic and corresponding to each of the four species identified by the Examiner: 1, 10 and 11; 13-19; 24-30; and 31-40.

Applicants affirm the election with traverse of the claims of Group I, claims 1-36 and 39-45, made in the telephone conversation with Applicants' representative of 7 December 2007. Applicants traverse on the grounds that, due to substantial overlap in subject matter, examination of the claims of groups 1 and 2 together would not be an undue burden on the Examiner. Applicants also affirm election of the species (1) hematopoietic stem cells, (2) hydroxyurea, (3) EGLN, and (4) beta-thalassemia and sickle cell syndrome from each of the Examiner's categories 1 to 4 for examination. Claims encompassing the elected species are at least as follows: Claims 1, 25, 27, 28, and 36 for species category 1; claims 11, 19 and 20 for species category 2; claims 1-9 for species category 3; and claims 10-15, 28-33 and 39-43 for species category 4.

III. Double Patenting

The Examiner has provisionally rejected claims 1-16, 19-21, 23-27, and 39-43 under 35 U.S.C. § 101 as allegedly "claiming the same invention as that of claims 1-16, 17-24, 27-3[sic], and 34-54" of copending Application No. 11/348,294 (the '294 Application"). (Office Action, page 7.)

Applicants request clarification as to the exact claims in the present application that the Examiner asserts claim the same invention as the '294 Application. Moreover, in accordance with section 804(I)(B)(2) of the M.P.E.P., Applicants hereby request that this provisional statutory double patenting rejection be held in abeyance until this is the only rejection remaining in the subject application.

IV. Rejection of claims under 35 U.S.C. §112, 2nd paragraph

The Examiner rejected claims 11 and 39-43 under 35 U.S.C. §112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action, page 8.) Specifically, the Examiner stated that claim 11 is "drawn to a method" and claims 39-43 are drawn to the use of a medicament, but as "the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass." (Office Action, page 8.) As Applicants have canceled claims 39-43, the rejection is moot as it applies to these claims.

Applicants have amended claim 11 above to positively recite a step of administering a HIF prolyl hydroxylase inhibitor to a subject in order to treat a disorder associated with abnormal hemoglobin in the subject. Claim 11 sets forth steps involved in the method and is thus definite as to the encompassed process. As claim 11 is definite and claims 39-43 are canceled, Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §112, 2nd paragraph.

IV. Rejection of claims under 35 U.S.C. §101

The Examiner rejected claims 11 and 39-43 under 35 U.S.C. §101 because "the claimed recitation of a use (claims 39-43) or recitation of an end result of a method step (claim 11), without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101." (Office Action, page 8.) As Applicants have canceled claims 39-43, the rejection is moot as it applies to these claims.

As stated above, claim 11 as amended positively recites steps of the claimed process. As claim 11 as amended correctly recites a method step and claims 39-43 have been canceled, Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §101 as being improper process claims.

V. Rejections of claims under 35 U.S.C. §102

A. The Examiner rejected claims 1, 10, 11-16, 19-21 and 23-25 under 35 U.S.C. §102(b) as being anticipated by Tung et al., International Publication No. WO 97/12855, published 10 April 1997. The Examiner stated, "Tung et al. teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient ..., the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin[.]" (Office Action, page 9.) Further, the Examiner stated

"Tung et al teaches that the agent is administered in combination with a second therapeutic agent such as hydroxyurea ...." (Office Action, bridging pages 9 to 10.)

Tung et al. teach the use of butyrate prodrugs of lactic acid for increasing gamma globin and fetal hemoglobin in a patient. Tung et al. do not disclose the use of "a HIF prolyl hydroxylase inhibitor" as recited in amended claims 1, 10, 11, and 16. Tung et al. thus fail to anticipate claims 1, 10, 11, and 16, or dependent claims 12-15, 19-21 and 23-25, and Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(b) as being anticipated by Tung et al.

B. The Examiner rejected claims 1, 10, 11-16 and 21-26 under 35 U.S.C. §102(b) as being anticipated by Perrine, International Publication No. WO 93/18671, which published on 30 September 1993. The Examiner stated Perrine "teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient ..., the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin[.]" (Office Action, page 10.) Further, the Examiner stated Perrine "administers said agent to cells from erythroid progenitors from peripheral blood from patients having a betaglobin disorder, thus Perrine administers said agent ex vivo...." (Office Action, page 10.)

Perrine taught administering compositions of isobutyramide to stimulate production of fetal hemoglobin. Perrine did not disclose the use of "a HIF prolyl hydroxylase inhibitor" as recited in amended claims 1, 10, 11, and 16. Perrine thus fails to anticipate claims 1, 10, 11, and 16, or dependent claims 12-15 and 21-26, and Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(b) as being anticipated by Perrine.

C. The Examiner rejected claims 1, 10, 11-16, 21-33 and 36 under 35 U.S.C. §102(b) as being anticipated by Bohmer, International Publication No. WO 01/12784, which published on 22 February 2001. The Examiner stated Bohmer "teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient ..., the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin[.]" (Office Action, page 11.) Further, the Examiner stated Bohmer teaches "administering to a population of cells (such as hematopoietic stem cells) an agent which increase the number of fetal hemoglobin producing cells ... and transferring said cells into the subject ...." (Office Action, bridging pages 11 to 12.)

Bohmer teaches culturing erythroid progenitor cells in the presence of cytokine, particularly transforming growth factor (TGF)-ß, in an amount sufficient to increase the number of fetal hemoglobin producing erythroid cells in the culture. Bohmer does not teach or suggest the use of "a HIF prolyl hydroxylase inhibitor" as recited in amended claims 1, 10, 11, 16 and 28. Bohmer thus fails to anticipate claims 1, 10, 11, 16 and 28, or dependent claims 12-15, 21-27, 29-33 and 36, and Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(b) as being anticipated by Bohmer.

D. The Examiner rejected claims 1-16, 19 and 21-25 under 35 U.S.C. §102(b) as being anticipated by Klaus et al., International Publication No. WO 03/053997, which published on 3 July 2003, as evidenced by Pace et al. (Exp Hematol 28:283-293, 2000). The Examiner stated that

> Klaus teaches a method for increasing endogenous erythropoietin in vitro and in vivo by administering a compound which/agent which increase endogenous erythropoietin.... Erythropoietin increases expression of the gene encoding gamma globin thus increasing the level of fetal hemoglobin as evidenced by Pace et al.... Thus, said method of increasing endogenous erythropoietin of Klaus et al will increase endogenous gamma globin and thus increase fetal hemoglobin absent evidence to the contrary.

(Office Action, page 12.) As Applicants have canceled claims 6-8, the rejection is moot with respect to these claims.

Applicants have amended claims 1, 10, 11 and 16 above to specifically recite "administering ... a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding γ-globin." Neither Klaus et al. nor Pace et al. disclose that a HIF prolyl hydroxylase inhibitor would increase expression of a gene encoding γ-globin. Further, neither Klaus et al. nor Pace et al. disclose "administering ... a HIF prolyl hydroxylase inhibitor which increases expression of a gene encoding γ-globin" as recited in the present claims. Thus, Klaus et al., read alone or in view of Pace et al., does not anticipate claims 1, 10, 11 and 16 or dependent claims 2-5, 9, 12-15, 19 and 21-25. As claims 6-8 have been canceled and claims 1-5, 9-16, 19, and 21-25 are not anticipated by Klaus et al., Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. §102(b) as being anticipated by Klaus et al. as evidenced by Pace et al.

CONCLUSION

In view of the foregoing, Applicants submit that the claims are fully in condition for allowance and request early notification to that effect.

The Commissioner is hereby authorized to charge any necessary fees to Deposit Account No. 50-0811, referencing Docket No. FP0617 US.

Please call Applicants' representative at 650.866.7265 with any questions regarding this communication or the above-identified application.

Respectfully submitted,

Date: 5 Sept 2008

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